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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/518,223	12/15/2004	Ning Man Cheng	090923-0103	7018

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EXAMINER

CHOWDHURY, IQBAL HOSSAIN

ART UNIT	PAPER NUMBER
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1652

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09/18/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/518,223	Applicant(s) CHENG ET AL.	
	Examiner IQBAL H. CHOWDHURY	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 5/30/08; 1/27/08.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 24,27,28,38,39 and 42-46 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 28 and 44-46 is/are allowed.
- 6) ☒ Claim(s) 24,27,38,39 and 42 is/are rejected.
- 7) ☒ Claim(s) 43 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>3/17/08</u> . | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Claims 24, 27-28, 38-39, and 42-46 are currently pending.

The preliminary amendment filed on 5/30/2008, canceling claims 40-41 is acknowledged.

Claims 1-23, 25-26, and 29-37 were previously cancelled.

Claims 24, 27-28, 38-39 and 42-46 are under consideration and will be examined herein.

Election/Restriction

Applicant's election of species without traverse of protein of SEQ ID NO: 9 or a nucleic acid encoding SEQ ID NO: 9 in the communication filed on 5/30/2008 is acknowledged. Protein of SEQ ID NO: 3 or a nucleic acid encoding SEQ ID NO: 3 is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, but would be rejoin, if SEQ ID NO: 9 is allowable.

Claims 24, 27-28, 38-39 and 42-46 are present for examination.

Applicants' arguments filed on 5/30/2008 and 1/27/2008 have been fully considered but are not deemed persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim objections

Claim 24 is objected to in the recitation of "80-100% purity", which should be "80-100% purity as determined by gel chromatography and densitometry". Appropriate correction is required.

Withdrawn-Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Previous rejections of Claims 24, and 27-28 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement and scope of enablement issue are withdrawn in view of applicants amendment of claims and persuasive arguments.

Withdrawn-Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

Previous rejection of Claim 28 under 35 U.S.C. 102(e) as being anticipated by Tepic et al. (WO/2003/063780, publication 7/8/2003, claim priority of provisional application 60/350,971 filed on 1/25/2002, see IDS) is withdrawn in view of applicants antedating the Tepic et al. reference by submission of Declaration under 37 CFR 1.131 as evidence of reduction to practice on a date before January 25, 2002, which is earliest effective filing date of Tepic et al. (WO 03/063780 (PCT/US03/02342)).

Withdrawn-Claim Rejections - 35 USC § 103

Previous rejection Claims 24, 26-27, 32 and 35-36 under 35 U.S.C. 103(a) as being unpatentable over Tepic et al. (WO/2003/063780, publication 7/8/2003, claim priority of provisional application 60/350,971 filed on 1/25/2002, see IDS) in view of Ikemoto et al.

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(Expression of human liver arginase in *Escherichia coli*. Purification and properties of the product, *Biochem J.* 1990 Sep 15; 270(3): 697-703, see IDS) is withdrawn in view of applicants antedating the Tepic et al. reference by submission of Declaration under 37 CFR 1.131 as evidence of reduction to practice on a date before January 25, 2002, which is earliest effective filing date of Tepic et al. (WO 03/063780 (PCT/US03/02342)).

New-Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 24, 27, 38-39, and 42 are rejected under 35 U.S.C. 103 (a) as being obvious over Vockley et al. (Arginase II, US 6316,199 B1, issue date 11/13/2001, see IDS) in view of Mehvar

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et al. (Modulation of the pharmacokinetics and pharmacodynamics of proteins by polyethylene glycol conjugation, J Pharm Pharmaceut Sci, 3(1):125-136, 2000).

Instant claims are directed to a method of treating human liver, breast, colon or rectal malignancies comprising administering to a subject a modified, full-length human arginase I polypeptide of 80-100% purity, which is covalently linked to polyethylene glycol (PEG), wherein said arginase I polypeptide has the amino acid sequence of SEQ ID NO: 9 (encoded by nucleotide sequence of SEQ ID NO: 8), wherein the half-life of modified arginase is 3 days.

Vockley et al. teach human arginase II and I, wherein said arginase I is 100% identical to arginase I of SEQ ID BNO: 9 of the instant application, which degrade arginine to ornithine and urea, resulting in reducing the arginine level, and a method for treating human cancer including prostate cancer by administering arginase II polypeptide (see Col 3, line 37-38). Vockley et al. also teach recombinant expression of human arginase II, expression in Sf9, Cos and E. coli followed by purification by affinity chromatography due to the presence of HA tag (Example 3 and 4), which results substantial purified protein that is within the scope of 80-100% pure (see Col 11, line 55-66). Vockley et al. further teach a pharmaceutical composition comprising human arginase II for treating said cancer (see Col 3, line 13-17) and pegylated the said protein by treating with polyethylene glycol (PEG) to increase the half-life of the protein in serum and reduce the antigenicity to be an effective therapeutic composition for treating cancer (see Col 14, line 47-64). The composition of Vockley et al. does not comprise arginase I and Vockley et al. do not teach half-life of the pegylated arginase at least 3 days.

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Mehvar et al. teach the half-life of arginase protein of 12 hrs after pegylation with polyethylene glycol and further teach that said arginase conjugate increased the survival time in mice with Taper liver tumor (page 128, left column, line 3-8).

Vockley et al. teach arginase I and a method of treating cancer with arginase II, an isoform of arginase I having identical function of degrading arginine, wherein said arginase II is modified with PEG, which increased the half life arginase. Mehvar et al. also teach treating mice with arginase protein modified with PEG, which increased the half-life in mice to 12 hrs.

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention was made to replace arginase II with arginase I as taught by Vockley et al. and use the method of Vockley et al. to make a therapeutic composition comprising human arginase I pegylated with PEG as taught by Vockley et al. and Mehvar et al. for treating cancer by administering in a patient and monitoring arginine half-life of the pegylated arginase in the serum for 3 days (36 hrs) as Mehvar et al. teach pegylated arginase half-life is 12 hrs.

The substitution of arginase II by arginase I is obvious because the two enzymes have identical activity. See KSR Int'l Co. V. Teleflex, Inc. 82 USPQ2d 1385 (2007).

One of ordinary skill in the art would have been motivated to replace arginase II by arginase I in view of its identical activity to arginase II, which has been shown to use in treating cancer by reducing the arginine level because arginine is regarded as the cancer-causing chemical in vivo. One of ordinary skill in the art would have been motivated also to use pegylated arginase to increase the half-life of the enzyme for at least 3 days in serum to increase the effectiveness of the enzyme against malignant cell in order to treat cancer, since, Vockley et al. and Mehvar et al. clearly teach the increased half life of arginase protein by pegylation, which

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is effective for the treatment and one ordinary skill in the art would be able to increase the half life of pegylated arginase I to 3 days by optimizing the pegylation of arginase I by using high molecular weight PEG and monitoring arginase concentration in the serum, which is a matter of routine experimentation and obvious to one of skilled artisan to obtain better results.

One of ordinary skill in the art would have a reasonable expectation of success because Vockley et al. could successfully used arginase II, which is an isoform of arginase I having identical function, i.e. arginine degrading activity for treating cancer.

Therefore, claims 24, 27, 38-39, and 42 would have been *prima facie* obvious to one of ordinary skill in the art.

Conclusion

Status of the claims:

Claims 24, 27-28, 38-39 and 42-46 are pending.

Claims 24, 27, 38-39, and 42 are rejected.

Claims 28 and 44-46 are allowed.

Claim 43 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Iqbal Chowdhury whose telephone number is 571-272-8137. The examiner can normally be reached on 9:00-5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nashaat T. Nashed can be reached on 571-272-0934. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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